Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1, 35–39, and 55–57 under 35 U.S.C. § 112 (1st para.) for lack of written description is respectfully traversed.

Claim 1 relates to an isolated DNA molecule from a Gram positive bacterium, the isolated DNA molecule comprising a coding region from a *dnaN* gene that encodes a polypeptide that has activity as a beta clamp and is capable of functionally interacting with a polymerase during DNA polymerization. The specification clearly discloses that *dnaN* encodes a beta clamp useful for highly processive DNA replication, and sets forth the nucleotide sequence for two *dnaN* genes, one from *Streptococcus pyogenes* and the other from *Staphylococcus aureus*, as well as the amino acid sequences of the encoded beta clamp proteins. The disclosure of the two *dnaN* molecules, plus the demonstration of relatedness of β homologs from other Gram positive bacteria (shown in Figure 20E) demonstrates that the applicants were in possession of the claimed invention. The Examples further support the recited β clamp activity, where it is shown that *Staph. aureus* β interacts with both *Staph. aureus* and *E. coli* (a Gram negative) polymerases on linear DNA (*see* Example 9 and Figure 5A) but only *Staph. aureus* polymerase on circular DNA (*see* Example 10 and Figure 5B), and *Strep. pyogenes* β interacts with *Strep. pyogenes* polymerase (*see* Examples 31, 34, and 35).

The basis of rejection concerning the recitation of fragments is overcome by the above amendments.

For all these reasons, the rejection of claims 1, 35–39, and 55–57 for lack of written description is improper and should be withdrawn.

The rejection of claims 1, 35–39, and 55–57 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

The PTO appears to base this rejection on three issues: (1) that the specification is enabling with respect to the *Strep. pyogenes dnaN* gene, but is not enabling for *dnaN* genes from other Gram positive bacteria; (2) the specification does not describe various uses for Gram positive bacterial *dnaN* and beta clamps; and (3) the claim scope encompasses all *dnaN* fragments.

With respect to the first issue, *Staph. aureus* and *Strep. pyogenes dnaN* coding regions are representative of Gram positive *dnaN* coding regions generally. As disclosed in

Examples 9–11 (*Staph. aureus*) and Examples 26, 31, and 34–35 (*Strep. pyogenes*), the proteins encoded by *Staph. aureus* and *Strep. pyogenes dnaN* function effectively as beta clamps with Pol III-L (α-large) Gram positive polymerases. Moreover, as shown in Figure 20E, the *Strep. pyogenes* beta protein is shown to be between 19 and 51% homologous to the beta proteins of a number of other Gram positive and Gram negative bacteria. Given the demonstrated ability of the beta proteins encoded by *Staph. aureus* and *Strep. pyogenes dnaN* to functionally interact with Gram positive polymerases, and the degree of homology between the various Gram positive beta proteins, *Strep. pyogenes* and *Staph. aureus dnaN* are representative of Gram positive *dnaN* coding regions generally.

With respect to the second issue, the PTO's observation (even if true, which applicants do not concede) is irrelevant to the enablement of claims 1, 35–39, and 55–57 because the claims are directed to isolated DNA molecules, not to methods of their use. Nevertheless, as noted above, the application does identify the activity and use of the β proteins encoded by the claimed nucleic acids. Specifically, the above-noted examples confirm the utility of the encoded beta protein to enhance replicative efficiency of a type III polymerase. This can clearly be used in *ex vivo* polymerase reactions. Moreover, the specification recites that beta proteins can be employed in one or more assays to identify new pharmaceutical agents that can disrupt interaction between the replication enzyme components (beta with either the polymerase or the gamma complex) and/or with DNA substrate. Specific assays are described at pages 77–83 of the present application (e.g., method to identify chemicals that inhibit the activity of the three-component polymerase, method to identify candidate pharmaceuticals that inhibit the activity of a clamp loader complex and a beta subunit in stimulating the DNA polymerase, method to identify chemicals that inhibit the ability of a beta subunit and a DNA polymerase to interact physically, method to identify chemicals that inhibit the ability of a beta subunit and a tau complex to interact, method to identify chemicals that inhibit the ability of a tau complex to assemble a beta subunit onto a DNA molecule, method to identify chemicals that inhibit the ability of a tau complex to disassemble a beta subunit from a DNA molecule, method to identify chemicals that disassemble a beta subunit from a DNA molecule, etc.). Regardless of the assay, the function of replication proteins is quantified in the presence of different chemical compounds. Chemical compounds that inhibit the function can be considered candidate antibiotics.

The basis of rejection concerning the recitation of fragments is overcome by the above amendments.

For these reasons the rejection of claims 1, 35–39, and 55–57 for lack of enablement is improper and should be withdrawn.

The rejection of claims 1, 35–38, and 55–56 under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 6,699,703 to Doucette-Stamm et al. ("Doucette-Stamm") is respectfully traversed.

The PTO has cited Doucette-Stamm for its disclosure of SEQ ID NO: 1744 (1137 nt in length), which is a portion of SEQ ID NO: 2550 (1215 nt in length) of the parent case, which larger sequence is identified as the beta subunit of DNA polymerase III from *Strep. pneumoniae*. Doucette-Stamm claims priority to July 2, 1997.

As demonstrated by the accompanying Declaration of Michael E. O'Donnell under 37 CFR § 1.131, the applicants had invented the presently claimed subject matter prior to July 2, 1997. In particular, applicants had isolated and cloned the *Staph. aureus dnaN* gene, and expressed the encoded beta protein prior to July 2, 1997. Based on the homology between *Staph. aureus* and *Strep. pyogenes* (and other Gram positive bacteria), discussed above, possession of the *Staph. aureus dnaN* gene is sufficient to establish possession of the presently claimed genus prior to July 2, 1997.

Because Doucette-Stamm is not available prior art under 35 U.S.C. § 102(e), the rejection of claims 1, 35–38, and 55–56 for anticipation by Doucette-Stamm should be withdrawn.

The rejection of claims 1 and 35 under 35 U.S.C. § 102(b) for anticipation by Moriya et al., *Nucleic Acids Research*, 13:2251–2265 (1985) ("Moriya") is respectfully traversed in view of the above amendments. Moriya relates in part to the identification and sequencing of the *Bacillus subtilis* open reading frame ORF378, which is disclosed to be homologous to the *E. coli dnaN* open reading frame. Because claims 1 and 35, as presently recited, do not read on Moriya, Moriya cannot anticipate the presently claimed subject matter. Therefore, the rejection of claims 1 and 35 for anticipation by Moriya should be withdrawn.

The rejection of claims 1, 35–38, and 55–56 under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 6,245,906 to Ueyama et al. ("Ueyama") is respectfully traversed. Ueyama, which issued from U.S. Patent Application No. 09/381,862, filed January 11, 2000, is not available prior art. As discussed above, the claimed subject matter has a priority date prior to July 2, 1997, when the *Staph. aureus dnaN* gene was isolated and cloned, and in any event no later than July 29, 1999, the filing date of the priority application (U.S. Patent Application Serial No. 60/146,178) in which the *Strep. pyogenes dnaN* gene was

disclosed. Both dates are well before Ueyama's apparent 102(e) date of January 11, 2000. The rejection of claims 1, 35–38, and 55–56 for anticipation by Ueyama, therefore, is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: December 5, 2005

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CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

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December 5, 2005

Edwin V. Merkel